REMARKS

Claims 1-22, 24-31, and 33-36 are pending in this application. Claims 23 and 32 have been canceled. Claims 1, 5, 6, 7, 19, 21 and 31 have been amended. The amendments made herein to the claims do not incorporate new matter into the application as originally filed. Support for the amendments can be found in the drawings and throughout the Specification.

OBJECTIONS

The Examiner objected to the drawings because reference characters "64" and "52" have both been used to designate microbeads. The Examiner also objected to the drawing because Figure 5 did not include the references mentioned in the description-66, 68, 70, 74, and 74. Also, because the use of the designator "6" on Figure 3 and "5" on Figure 4 is not used in the description.

The Specification has been amended on page 18, line 24 to replace the only occurrence of "52" with "64." The Specification has also been amended on page 18, line 28 to replace the only occurrence of "5" with "3". A review of the Specification will indicate that, except for the one typographical error, the microbeads are identified by 64. A review of the drawings will also indicate that Figure 3, not Figure 5, has the designations 66, 68, 70, 74, and 74. Finally, a review of the drawings will indicate that Figure 4 is a top view of the float of Figure 3. Figure 4 is also represented as a cross-section of Figure 5 as identified in the Specification with the designation 5-5. Figure 3 has been amended to include the identifier 58, which is the inclined trailing end of the float, to more clearly represent the drawings. Support for this amendment can be found on page 19, line 8. The Examiners objections have been obviated because the Applicants have

submitted corrected drawings and amended the Specification to reference the appropriate designations and figures. Attached to this Amendment for the Examiner's consideration is a page with a corrected Figure 3.

REJECTIONS

Rejection of claims 3, 5, 7-12, 14, 18, 21, 23, 32 and 35 under 35 U.S.C. § 112, 2nd paragraph

The Examiner has rejected claims 3, 5, 7-12, 14, 18, 21, 23, 32 and 35 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. More specifically, the Examiner states:

> a) Claim 1 is incomplete because it lacks a correlation step.
> b) The phrase "axial through passage" of Claim 5 is vague and indefinite because it is unclear of what an axial through passage of the float is. Is the passage part of the tube or the float?
> c) The phrase "having a through passage" of Claims 19 and 31 is vague and indefinite because it is unclear of who has the through passage. Is the passage part of the tube or the float? (See the Official Action at page 3, paragraph 7.)

Applicants respectfully traverse this rejection.

Claim 1 has been amended to correlate the steps of the method. The Specification at page 10, lines 6-7, and also at page 10, lines 23-26, indicates that the axial through passage is a part of the float. Applicants have amended claims 5, 19 and 31 to advance prosecution. Withdrawal and recondsideration of the rejection is requested.

Rejection of claims 1, 4-7, and 15-17 under 35 U.S.C. § 102 (b) over U.S. Patent 5,635,362

The Examiner has rejected claims 1, 4-7, and 15-17 under 35 U.S.C. § 102 (b) as being anticipated by U.S. Patent 5,635,362 (Levine et al.) (hereinafter "Levine '362"). Applicants respectfully traverse the rejection.

Levine '362 teaches a one-step method for determining the presence or absence of a target analyte in a biological sample using target-analyte capture bodies that settle into predetermined locations within a transparent tube and labeling of the captured analyte. (See col. 1, lines 8-17.) The float of Levine '362 does not have a bore.

The present invention discloses and claims a method for separating a targeted component from a sample. The method entails mixing the sample of interest with antibodies that have an affinity for the target in a container that has a focusing device with a passage for receiving and elongating layers of the sample and centrifuging the container and sample to separate the components of the sample and isolate and remove the targeted component.

Levine '362 does not teach the removal of the targeted component. Further, the float of Levine '362 does not contain a bore or other passage that receives and elongates the layers of the sample. As stated by the Court of Appeals for the Federal Circuit in the case of *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Company et al.*, 221 USPQ 481 (1984):

> Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 218 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the trier of fact must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH*, supra; *Kalman*, supra.

The present claims do not contain every element of the prior art reference. As such, the reference discussed above does not anticipate the claimed invention. Withdrawal and reconsideration of the rejection is respectfully requested.

Rejection of claims 2-3, 19-20, 22, 24-27, 30, 31, 33-34 and 36 under 35 U.S.C. § 103 (a) over Levine '362 in view of U.S. Patent 5,393,674 (Levine et al.)

The Examiner has rejected claims 2-3, 19-20, 22, 24-27, 30, 31, 33-34 and 36 under 35 U.S.C. § 103 (a) as being unpatentable over Levine '362 in view of U.S. Patent 5,393,674 by Levine et al. (hereinafter Levine '674). The Examiner states, "It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Levine #1 [Levine '362] by incorporating the method step removing the target component as taught by Levine #2 [Levine '674] because it would provide the advantage of performing multiple methods such as cell concentration, assay, and harvesting in a unitary sealed tube (Levine #2: col. 1, lines 41-57)." Applicants respectfully traverse this rejection.

Levine '362 differs from the present invention in that it fails to disclose the density, size and type of bead. The present invention discloses and claims a method for harvesting a target component using particulate carriers at a certain density, size and type. The combined references fail to teach every limitation of the claimed invention. Applicants request withdrawal and reconsideration of the rejection.

Rejection of claims 8-12, 14, 18, 21, 23, 28-29, 32, and 35 under 35 U.S.C. § 103 (a) over Levine '362 in view of U.S. Patent 5,474,687 (Van Vlasselaer)

The Examiner has rejected claims 8-12, 14, 18, 21, 23, 28-29, 32, and 35 under 35 U.S.C. § 103 (a) over Levine '362 in view of U.S. Patent 5,474,687 by Van Vlasselaer (hereinafter "Van Vlasselear '687"). The Examiner states, "It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the density beads of Levine with those density beads of Levine of Van Vlasselear. One of ordinary skill would be motivated because both Levine and Van Vlasselaer teaches methods of providing accurate and reproducible cell separation layers. . . . One would have had reasonable expectation of success using the beads of Van Vlasselaer with the method of Levine because both use the similar method to achieve cell separation" (See Official Action, page 8, lines 4-15.) Applicants respectfully reverse the rejection.

To establish a case of obviousness, in addition to a motivation to combine the teachings of the references and a reasonable expectation of success, the prior art references must teach or suggest all the claim limitations. The combined teachings of Levine '362 and Van Vlasselaer '687 do not teach the limitations of the present invention. Neither Levine '362 nor Van Vlasselaer '687 discloses a bore or other passage for receiving and elongating the layers of the sample. As explained at page 10, lines 3-11, the target component of the present invention collects in the axial bore. As the references fail to teach all of the limitations of the claimed invention, the present invention is not obvious. Withdrawal and reconsideration of the rejection is requested.

CONCLUSION

Applicants believe the present invention to be novel and unobvious and respectfully request a Notice of Allowance clearly stating the grounds of patentability. However, should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Jaconda Wagner (Reg. No. 42,207) at the telephone number below, to conduct an interview in an effort to expedite prosecution in connection with the present application. Please note that attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-1666 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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60500v1
Attachment: Version with Markings to Show Changes Made
Amended Figure 3

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

-- In this embodiment, a biological sample, such as a blood sample, is placed in container 32. An amount of microbeads 64 having an affinity binding agent for a target component is mixed with the sample. Container 32 is then centrifuged as in the previous embodiment to collect the microbeads 64 with the captured target component in longitudinal channels 62 of float 48. Microbeads 64 [52] and the captured target component can then be analyzed by visualizing the target component within container 32 by microscopy methods as known in the art.

In the embodiments shown in Figure 3 [5], the blood sample after centrifuging separates into a layer of red blood cells 66, a granulocyte cell fraction layer 68, a mononuclear cell fraction 70, a plasma fraction 72 and a platelet/plasma interface 74. In a positive selection process, microbeads "69have an affinity for the target compound and collect in channels 62. Alternatively, microbeads 64 can have an affinity for white and/ or red blood cells in a negative selection process Channels 62 are formed between ribs 60 and are enclosed by top wall 34 of container 32. Inclined leading edge 56 and inclined trailing edge 58 divert the sample through channels 62 as float 48 slides through container 32. Microbeads 64 are retained in a thin layer in channels 62 close to top wall 34 of container 32 so that the microbeads 64 can be visualized through top wall 34 by microscopy or other analytical methods as known in the art. Preferably, front wall 3 of container 32 is substantially flat to prevent the optical distortion normally associated with cylindrical containers.--

IN THE CLAIMS:

The claims have been amended as follows:

1. A method of separating ~~harvesting~~ components from a sample material, said method comprising the steps of:

providing a sample material in a sampling container, said sampling container having a focusing device with a passage for receiving and elongating layers of sample components to be harvested from said sample,

providing at least one antibody in said sampling container, and mixing said antibody with said sample, wherein said antibody has an affinity for binding with at least one substance in said sample, and

centrifuging said container and sample at sufficient G forces to separate components of said sample and to force a target component from said sample into said passage.

5. The method of claim 1, wherein said container is a tube having an inner surface, and said focusing device is a float having an axial passage wherein said float has an outer surface complementing ~~said~~ the inner surface of ~~said~~ the tube ~~and having an axial through passage~~.

6. The method of claim 5, further comprising providing a particulate carrier and mixing said particulate carrier with said sample, wherein ~~said~~ at least one antibody is bound to a surface of said particulate carrier.

7. The method of claim 6, wherein said particulate carrier comprises an effective amount of microbeads having a density greater than a density of white blood cells and wherein said antibody has an affinity for white blood cells.

19. A method of harvesting a target component from a sample, said method comprising the steps of:

providing a sample in a sampling tube, said sampling tube containing a float dimensioned to fit within said sampling tube, wherein said float has an axial ~~and having a through~~ passage for receiving and elongating layers of blood constituents to be harvested from said sample,

mixing said sample with at least one particulate carrier having a density of about 1.0 to 1.06 g/cc, size of about 4 microns to 5 microns and containing an antibody having a binding affinity for a specific sample constituent,

centrifuging said tube and sample at sufficient G forces to move said float toward one end of said tube and to force a target component from said sample into said through passage, and

removing said target component from said through passage.

21. The method of claim 19, wherein said particulate carrier comprises microbeads ~~having a density of about 1.00 to about 1.06 g/cc~~.

31. A method of harvesting a target component from a whole blood sample, said method comprising the steps of:

providing a whole blood sample in a sampling tube, said sampling tube containing a float dimensioned to fit within said sampling tube and ~~having a through~~ said float has an axial passage for receiving and elongating layers of blood constituents to be harvested from said sample,

mixing said sample with an amount of first carrier beads having a density of about 1.0 to 1.06 g/cc and a coating of a first antibody that has a binding affinity for a target constituent in said sample, and an amount of second carrier beads having a coating of said second antibody that has a binding affinity for white blood cells,

centrifuging said tube and sample at sufficient G forces to move said float toward one end of said tube and to force said first carrier beads and target constituent into said through passage, and

removing said first carrier beads and target constituent from said through passage.